

# Effect of Intrathecal Dexmedetomidine as Adjuvant to Hyperbaric Bupivacaine for Total Abdominal Hysterectomy: A Double Blind Control Study

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## Abstract

**Aims and Objectives:** The aim of this study is to evaluate the effects of Dexmedetomidine as intrathecal adjuvant to Bupivacaine in spinal anaesthesia on the onset and duration of sensory and motor block in Total Abdominal Hysterectomy (TAH).

**Materials and Method:** Sixty patients of ASA status I and II posted for Total Abdominal Hysterectomy were randomly divided into three groups. Group C were administered Hyperbaric Bupivacaine 15mg plus 0.5 ml normal saline, Group D was administered Hyperbaric Bupivacaine 15mg + Dexmedetomidine 10µg in 0.5 ml normal saline. Duration and quality of sensory and motor block were assessed.

**Results:** Sensory and motor block in group D patients were longer than group C patients.

**Conclusion:** Intrathecal dexmedetomidine when added to bupivacaine heavy (0.5%) provide better and prolonged analgesia.

**Keyword:** Total Abdominal Hysterectomy, Bupivacaine, Intrathecal, Dexmedetomidine.

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## Introduction

Subarachnoid block is one of the most commonly used techniques for Total Abdominal Hysterectomy<sup>1</sup>. It can also be done with general anaesthesia, epidural anaesthesia. Perioperative pain control is a major problem in these surgeries because of relatively short duration of action of local anaesthetics, so early analgesic drugs or intervention is needed in the postoperative period. A number of adjuvants, such as clonidine and midazolam, and opioid's have been studied to prolong the effect of spinal anaesthesia<sup>2-5</sup>. Now a days, although fentanyl is used commonly but its intrathecal use has been shown to be associated with side effects like pruritus and respiratory depression<sup>6</sup>.

Dexmedetomidine, a new highly selective  $\alpha_2$ -agonist, is under evaluation as a neuroaxial

adjuvant as it provides stable hemodynamic conditions, good quality of intraoperative and prolonged postoperative analgesia with minimal side effects. As because its effect on spinal  $\alpha_2$  receptors, dexmedetomidine mediates its analgesic effects. Based on earlier human studies, it has been shown that a low dose of 10 µg, dexmedetomidine provides a prolonged anaesthesia and good quality postoperative analgesia when used as an intrathecal adjuvant to bupivacaine with minimal effects on the hemodynamic status of the patient<sup>7-9</sup>.

Therefore, our present study is being undertaken to evaluate the effects of dexmedetomidine as intrathecal adjuvants to bupivacaine.

## Methods

This randomized prospective clinical study was carried out in the department of Anaesthesia

Analgesia and SICU, BIRDEM General Hospital, Shahbag Dhaka. The approval of the Hospital Ethical Committee was duly taken before carrying out the study. Informed consent was taken from patients from July 2016 to June 2017. Sixty women aged between 35-60 years and weight between 50-70 kg, height of 150 cm to 180 cm of ASA physical status I and II with Mallampatti grade I and II scheduled for elective TAH was included. Patient with history of Diabetics or hypertension were also included in our study. Exclusion criteria were patients presenting with known contraindications to spinal anaesthesia. Patients on therapy with adrenergic receptor antagonist, calcium channel blocker, ACE inhibitor, with history of heart block or dysrhythmia, hypersensitivity to any of the study drugs and who refused to consent to be part of study are also excluded. The study population was randomized using random number table generated from computer software. Random intervention assignment slip was placed in serially numbered opaque and sealed envelopes. These envelopes were opened following enrolment of the case. After recruitment 60 patients were randomly divided into two groups (n= 30) patients each. Patients in group C received Hyperbaric Bupivacaine 15mg plus 0.5 ml normal saline, group D Hyperbaric Bupivacaine 15mg + Dexmedetomidine 10 µg in 0.5 ml normal saline intrathecally.

All the patients were kept for 10 hours fasting prior to surgery. Anti HTN were continued but morning insulin were omitted. Tablet Alprazolam (0.25 mg) was given as a premedication a night prior to surgery. Preloading was done with Ringer lactate solution (10 ml/kg body weight). Routine monitoring including non-invasive blood pressure (NIBP), ECG, heart rate and pulse oximetry was done.

Under proper aseptic conditions, spinal anaesthesia was given at the level of L3-L4 interspace in sitting position using a midline approach by a 25G Quincke spinal needle. The drug was injected slowly over 10-15 seconds with the bevel of the needle pointing upwards and all patients were made supine immediately. All patients received supplemental oxygen via mask (4 l/min).

The intrathecal drug formula was prepared by a separate anaesthesiologist under strict aseptic

conditions. The anaesthesiologist who administered anaesthesia was blinded to the group allocation. After administering anaesthesia the vital signs of the patient were recorded. Vitals were recorded every 2 minutes up to the 10th minute and every 5 minutes thereafter up to 20 minutes. Beyond 20 minutes the vitals were recorded every 20 minutes till the time of discharge from PACU (Post Anaesthesia Care Unit).

The sensory dermatome level was assessed by loss of pin prick sensation to a 23 G hypodermic needle.

The motor dermatome level was assessed according to the Bromage<sup>6</sup> Scale:

- Bromage 0- Patient able to move hip, knee and ankle.
- Bromage 1- Patient unable to move hip, but able to move knee and ankle.
- Bromage 2- Patient unable to move hip and knee but able to move the ankle.
- Bromage 3- Patient unable to move hip, knee and ankle.

Time to reach the sensory block up to highest dermatome level and motor block of bromage 3 level was noted. On achieving T6 sensory blocked level, the surgical procedure was carried out. Sensory and motor status was assessed prior to the spinal injection. After spinal injection every 2 minutes for the first 10 minutes, every 5 minutes for the next 10 minutes and thereafter every 20 minutes until the time to regression of sensory level to dermatome S2 and motor scale to bromage 0 was noted in PACU. All durations were calculated taking the spinal injection time as time zero. If the sensory levels were not equal bilaterally the higher dermatome level was used for statistical analysis. Sedation was assessed by using Modified Ramsay sedation score each time the vitals were noted.

#### **Modified Ramsay sedation scale<sup>9</sup>:**

1. Anxious, Agitated, Restless.
2. Cooperative, Oriented, Tranquil.
3. Responds to commands only.
4. Brisk response to light glabellar tap or loud noise.
5. Sluggish response to light glabellar tap or loud noise.
6. No Response

Postoperatively, the pain scoring was done by using visual analog scale (VAS)<sup>10</sup>. In it 0 = no pain, 10 = sever pain). Also the vital recordings of the study until the patient was discharged from PACU. Time of administering the first dose of rescue analgesia was noted. Paracetamol was given intravenous as rescue analgesia when VAS was greater than 4.

For the purpose of the study hypotension was defined as a decrease in systolic blood pressure more than 30% of the baseline value or fall below 90 mmHg, which was treated by inj. Ephedrine Hydrochloride 5 mg iv. incremental and fluid infusion. Bradycardia was defined as heart rate less than 60/min but the intervention with iv atropine 0.6mg was done only when heart rate fell below 50/min.

Side effects including nausea, vomiting, bradycardia, hypotension, pruritus, respiratory depression, shivering were assessed both intra-operatively as well as post-operatively. All the patients were examined by the anaesthesiologist up to 24 hours of the spinal block and were assessed for any postdural puncture headache or transient neurologic symptoms. Hemodynamic status of the patient, sedation score and side effects if any were noted.

All data were collected in a pre-designed data collection form. Results were compiled and analyzed using student's t test or Chi square test, Fisher exact test. P value <0.05 was considered statistically significant. The statistical analysis was done by using software SPSS (Statistical Package for Social Sciences) version 16 and Microsoft excel 2013. And we use web site <https://www.graphpad.com/quickcalcs>, <https://www.socscistatistics.com/tests/>

## Results

Both groups were comparable as regard to age, height and weight. There were no significant differences in heart rate, MAP, SPO2 between the groups. Intergroup analysis showed a statistically significant difference in the highest level of sensory blockade amongst group C and D (p = 0.004). Two segment regression time was more in dexmedetomidine group in comparison to control group.

Onset time to both sensory and motor block was faster on group D than group C. Regression time of motor block to bromage 0 was slow and time to rescue analgesia was longer in dexmedetomidine group in comparison to control groups. Sedation score was more in dexmedetomidine group. VAS score was lower in dexmedetomidine group than control groups. In our study the incidence of bradycardia, hypotension, nausea, vomiting, shivering was not statistically significant.

**Table I** Demographic profile

Parameters	Group C	Group D	P value
Age (years)	39.16±10.12	43.6±10.5	0.100
Weight (kg)	56.87±7.20	56±7.82	0.655
Height (cm)	156.47±6.40	158.43±5.92	0.223
ASA(I:II)	21:9	18:12	0.416
Duration of surgery (min)	98±17.84	97.67±15.24	0.938

Values were expressed as mean±SD. Data were analyzed by student's- t test. ASA grading done by chi-square test. Values were regarded as significant if p< 0.05.

**Table II** Characteristics of spinal block

Variable (min)	Group C	Group D	P value
Time of onset of sensory block	2.94±0.44	2.69±0.63	0.08
Time of onset of motor block	3.61±0.65	3.30±0.57	0.054
Onset time to reach T6 level	8.11±1.09	6.22±0.42	0.0001
Time of 2 segment regression	94.1±12.2	396.67±24.12	0.0001
Time of regression to S1	220.2±50.4	380.6±48.2	0.0001
Time of regression to Bromage 0	145±23.6	386±30.6	0.0001
Time to rescue analgesia	203.2±27.1	312±48.6	0.0001

Values were expressed as mean±SD. Data were analyzed by student's t -test. Values were regarded as significant if p< 0.05.

**Table-III** Highest dermatome level of sensory block

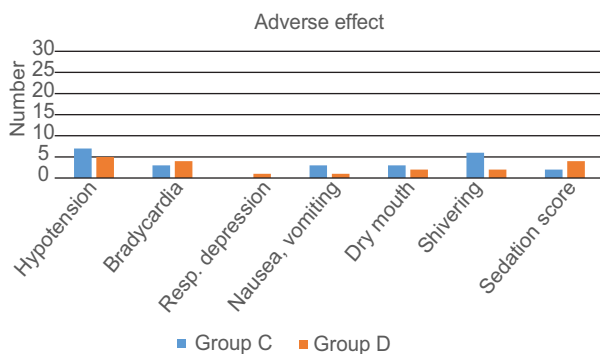
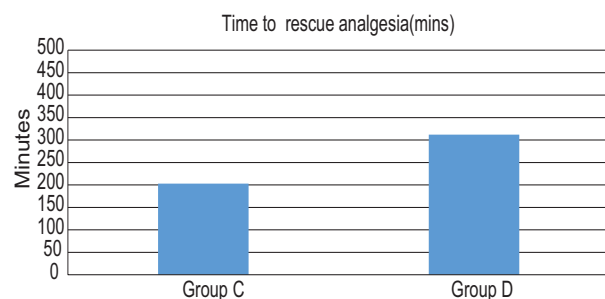
Highest level of sensory dermatome	Group C	Group D	Total
T4	4	9	13
T5	10	18	28
T6	16	3	19

Data were analyzed by AVONA -test. Values were significant if  $p < 0.05$ . ( $p = 0.004$ ).

**Table IV** Adverse effect of spinal block, (values are numbers)

Adverse effect	Group C	Group D	P value
Hypotension	7(23%)	5(16.66%)	0.518
Bradycardia	3(10%)	4(13.33%)	0.687
Resp. depression	0	1(3.33%)	>.05
Nausea, vomiting	3(10%)	1(3.33)	0.30
Dry mouth	3(10%)	2(6.66%)	0.640
Shivering	6(20%)	2(6.66%)	0.128
Sedation	2(6.66%)	4(13.33%)	0.389

Results were expressed in number and percentages in parentheses. Data were analyzed by chi-square test, Fisher exact test. Values were regarded as significant if  $p < 0.05$ .

**Fig 1** Showing adverse effect in both group**Fig 2** Time of first rescue analgesia (if VAS  $\geq 4$ )

## Discussion

The results of our study show that the supplementation of intrathecal bupivacaine with 10 µg dexmedetomidine significantly prolonged both sensory and motor block compared with control group. Patients in the group of dexmedetomidine had reduced post-operative pain scores and a longer pain free period than those who received spinal bupivacaine alone. No hemodynamic instability or severe adverse effects were reported in any group. Time taken to achieve peak level of sensory and motor blockade was earlier in dexmedetomidine group than other group.

Kanazi et al. used a small dose of dexmedetomidine (3mcg) with bupivacaine intrathecally in humans. They found shorter onset of motor block and prolongation in the duration of motor and sensory block with haemodynamic stability and lack of sedation<sup>11</sup>. And that is similar in our study where we did with dexmedetomidine 10 µg. Our study were also similar with the study of Al-Mustafa M M et al.<sup>12</sup>. They studied the effect of adding different doses of dexmedetomidine (5µg or 10µg) to bupivacaine (12.5mg) for neuroaxial

anaesthesia in urological procedure. They observed that dexmedetomidine prolongs the duration of spinal anaesthesia in dose-dependent manner.

El-Hennawy AM et al<sup>13</sup> found that addition of clonidine or dexmedetomidine to bupivacaine prolongs caudal analgesia in children. Alka Shah et al.<sup>14</sup> studied Hemodynamic effects of intrathecal dexmedetomidine added to ropivacaine intraoperatively and found that it prolonged the postoperative analgesia. Gehan A. Tarbeeh et al.<sup>15</sup> studied the effects of intrathecal bupivacaine-fentanyl versus bupivacaine dexmedetomidine diabetic surgical patients and concluded that dexmedetomidine produced better block characteristics. This was similar to our study in which dexmedetomidine group showed a statistically significant prolongation of both sensory and motor regression when compared to bupivacaine alone group.

Al Ghanem et al<sup>16</sup> conducted a three group study as- control, dexmedetomidine, fentanyl and observed that the onset time of bromage 3 motor block was also not different between dexmedetomidine and fentanyl group. Regarding time taken to achieve peak motor blockade there was no statistically significant difference was seen amongst all the three groups. The time to regression of sensory block to S<sub>1</sub> segment was significantly longer in dexmedetomidine group than in fentanyl group & control group (p < 0.001). The regression time to reach bromage 0 in dexmedetomidine group was significantly longer than that for fentanyl group (p < 0.001). In our study we also found statistical significant difference (p < 0.001) in both group. Jain et al<sup>17</sup> studied the perioperative effect of epidural dexmedetomidine with intrathecal bupivacaine on hemodynamic parameter and quality of analgesia and found that it is better than other adjuvants.

Bradycardia was seen in total number of 7 patients in our study and was more in dexmedetomidine group (4 patients) compared to control group, but it was transient and did not require any intervention. There was no statistically significant difference noted amongst the groups.

Nausea and vomiting was highest in control group (3 patients) and least in dexmedetomidine group.

It was also not statistically significant on analysis (p > 0.05). Sedation was more in dexmedetomidine group (4 patients) than control group though statistically not significant.

### Conclusion

We conclude from our study that supplementation of bupivacaine spinal block with a low dose of 10µg intrathecal dexmedetomidine produces a significantly longer duration of sensory and motor block than bupivacaine alone. It provides hemodynamically stable conditions, minimal side effects, and excellent quality of postoperative analgesia. Thus, 10 µg dexmedetomidine seems to be an attractive adjuvant in several gynecological operation as we conduct in total abdominal hysterectomy.

### Limitations of the study

This study was not without limitation. The limitations of the studies were as follows:

- Small sample size of the study population.
- It was a single centre study. Only patients admitted in BIRDEM General Hospital, Shahbag Dhaka were taken for the study. So this will not reflect the overall picture of the country. A large scale study needs to be conducted to reach to a definitive conclusion
- Study was conducted in a tertiary care hospital which may not represent primary or secondary centre.
- Sample were taken by purposive method in which question of personal biasness might arise.
- Others limitation were short duration of study and limited investigation facility.

### References:

1. Bauchat JR, et al. Evidence-based anesthesia for major gynecological surgery. *Anesthesiol Clin.* 2015 Mar; 33(1):173-207
2. Carollo DS, Nossaman BD, Ramadhyani U. Dexmedetomidine: a review of clinical applications. *Curr Opin Anesthesiol.* 2008; 21:457-461
3. Kaabachio, Zarghournia, Ouzeini R, Abdel Aziz A B, Chattaoui O, Kokki H 2007 Clonidine 1 microg/kg is a safe and effective



- adjuvant to plain bupivacaine in spinal anesthesia in adolescents *Anesth Analg*.105: 516–9
4. Ho K M, Ismail H 2008 Use of intrathecal midazolam to improve perioperative analgesia: a meta-analysis *Anaesth Intensive Care*.36:365–73
  5. Boussofara M, Carlès M, Raucoules-Aimé M, Sellam MR, Horn JL. Effects of intrathecal midazolam on postoperative analgesia when added to a bupivacaine-clonidine mixture. *Reg Anesth Pain Med* 2006; 31:501-5
  6. Gwirtz et.al. safety and efficacy of intrathecal opioid analgesia for acute postoperative pain: Seven years' experience with 5969 Surgical patients at Indiana university hospital. *Anesth Analg*.1999; 88:599-604
  7. Robert D. Sanders, Mervyn Maze. Alpha<sub>2</sub>-agonists and other sedatives and amnestics. In.: Alex S, Evers, Mervyn Maze, Evan D. Kharasch, editor .2nd edition. *Anesthetic Pharmacology* .Cambridge University Press; 2011.pp 478-492
  8. Anand VG, Kannan M, Thavamani A, Bridgit MJ. Effects of dexmedetomidine added to caudal ropivacaine in paediatric lower abdominal surgeries. *Indian J Anaesth*.2011; 55:340-6
  9. Panzer O, Moitra V, Roberet N Sladen. Pharmacology of sedative-analgesic agents – Dexmedetomidine, remifentanyl, ketamine, volatile anaesthetics and the role of Mu antagonists. *Critical Clin*.2009; 25:451-69.
  10. Stinson JN, Kavanagh T, Yamada J et al. Systematic review of the psychometric properties, interpretability and feasibility of self-report pain intensity measures for use in clinical trials in children and adolescents. *Pain*.2006;125(1-2):143–57.
  11. Kanazi GE, Aouad MT, Jabbour-Khoury SI, Al Jazzar MD, Alameddine MM, Al-Yaman R, et al. Effect of low-dose dexmedetomidine or clonidine on the characteristics of bupivacaine spinal block. *Acta Anaesthesiologica Scandinavica*.2006; 50(2):222-7.
  12. Al-Mustafa MM, Abu-Halaweh SA, Aloweidi AS, Murshidi MM, Ammari BA, Awwad ZM, et al. Effect of dexmedetomidine added to spinal bupivacaine for urological procedure. *Saudi Med J*.2009; 30:365-70.
  13. El-Hennawy AM, Abd-Elwahab. Addition of clonidine or dexmedetomidine to bupivacaine prolongs caudal analgesia in children. *Br J Anaesth*.2009; 103:268-74.
  14. Alka Shah, Ila Patel, Rachana Gandhi et al. Haemodynamic effects of intrathecal dexmedetomidine added to ropivacaine intraoperatively and for postoperative analgesia. *International Journal of Basic & Clinical Pharmacology* .January-February 2013: Vol 2: Issue 1, 26-29.
  15. Gehan A. Tarbeeh, Ayman A. Mohamed et al. Effects of intrathecal bupivacaine–fentanyl versus bupivacaine–dexmedetomidine in diabetic surgical patients. *Egyptian journal of Anaesthesia*.2013; 29, 13-18.
  16. Al-Ghanem SM, Massad IM, Al-Mustafa MM, Al-Zaben KR, Qudaisat IY, Qatawneh AM and Abu-Ali HM. Effect of Adding Dexmedetomidine versus Fentanyl to Intrathecal Bupivacaine on Spinal Block Characteristics in Gynecological Procedures: A Double Blind Controlled Study. *Am J Appl Sci*.2009; 6: 882-7.
  17. Jain D, Kumar D, Khan RM, Kumar N et al. Perioperative effect of epidural dexmedetomidine with intrathecal bupivacaine on haemodynamic parameter and quality of analgesia. *South Afr J Anaesth Analg*. 2012;18(1):105-109.